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Medication adherence in patients with cognitive disorders

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Abstract

Background: In aging population, managing multiple chronic diseases often results in polypharmacy and complex treatment regimens, which can challenge medication adherence. Cognitive decline, depression, and low health literacy may further hinder effective pharmacotherapy management. The aim was to assess the relationship between cognitive function, depressive symptoms, self-efficacy, health literacy, and polypharmacy with medication adherence among older adults, and explored patient strategies for managing medications.

Methods: A cross-sectional study was conducted among 212 primary care patients aged 60 years or older in Łódź, Poland. Standardized tools were used to measure cognition (MMSE), depression (GDS), self-efficacy (GSES), health literacy (HLS-EU-Q16), and adherence (ARMS). Logistic regression models were performed to identify independent predictors of adherence.

Results: Medication adherence decreased with worsening cognitive performance: 64.4% in patients with normal cognition, 56.1% with mild cognitive impairment, and 38.9% with dementia (p=0.010). Cognitive status (OR 0.34, 95% CI 0.15–0.78), male gender (OR 3.32, 95% CI 1.52–7.23), living alone (OR 0.48, 95% CI 0.23–0.98), polypharmacy (5–9 drugs daily: OR 0.34, 95% CI 0.16–0.71), and low health literacy (OR 0.37, 95% CI 0.17–0.81) were significantly associated with poorer adherence. Depression, number of specialists caring regularly for the patient, and use of pill organizers were not significantly associated predictors.

Conclusions: Medication adherence in older adults was strongly influenced by cognitive impairment, gender, health literacy and cohabitation. More research is necessary to determine whether regular cognitive screening in primary care, simplified pharmacotherapy regimens, and individualized adherence support for socially isolated or male patients could improve treatment outcomes in aging populations.

Keywords: Medication Adherence; Cognitive Dysfunction; Dementia; Polypharmacy; Older Adults; Aged; Health Literacy; Patient Compliance;

1 Background

In an aging population, people living with more than one chronic disease are the norm rather than the exception (1). Having multiple chronic conditions often leads to poorer health and significantly raises the overall cost of treatment. It also tends to result in more frequent hospital admissions and greater demand for medical services (2-4). With increasing age, the prevalence of chronic diseases rises, leading to a corresponding increase in the number of medications that patients are required to take. This growing treatment burden is further complicated by age-related cognitive decline, including memory impairment, which can negatively impact medication adherence and overall health management (5-8).

The increased number of medications prescribed to patients often results in polypharmacy, defined as the regular use of five or more medications simultaneously [9]. While polypharmacy can be clinically appropriate in many cases, it is also associated with an elevated risk of adverse drug reactions, drug-drug interactions, reduced medication adherence, and increased healthcare utilization (10-13).

However, medication adherence is shaped by many other factors as well. These include the patient's cognitive abilities (such as memory and attention), overall physical health, personal beliefs and attitudes toward medications, and the level of support they receive from family or caregivers. Adherence may also be affected by how complex the treatment plan is, for instance, how many medications the patient needs to take and how often, as well as by side effects and practical barriers, such as the cost of treatment or difficulty accessing healthcare services (14-19).

Although substantial research has addressed medication adherence in older adults, ongoing investigation remains necessary due to persistent and evolving challenges. The prevalence of multimorbidity and polypharmacy in this population is high, with more than half of older adults with hyperpolypharmacy (≥10 medications) demonstrating suboptimal adherence; the risk of poor adherence increases with the number of comorbidities and medication burden, underscoring the complexity of managing multiple chronic conditions [20-21]. Patterns of digital exclusion are also changing: while some older adults continue to face barriers to technology use, an increasing proportion are adopting digital tools and technology-mediated strategies, such as electronic reminders and smartphone applications, to support medication adherence. However, the effectiveness of these interventions is heterogeneous and depends on individual digital literacy and access, highlighting the need for further research to identify optimal approaches for diverse subgroups of older adults.[22-23]

Additionally, the use of combination drugs to reduce pill burden is an emerging strategy that may improve adherence, but its impact on older adults' understanding and management of their regimens is not fully understood and warrants further study.[24]

Given these dynamic factors - multimorbidity, evolving technology use, and changes in pharmacotherapy - medication adherence in ageing populations is not static and requires continued, targeted research to ensure safe and effective care [25-26].

Therefore, in order to broaden research on modifiable barriers to medication adherence in older adults, this study aimed to analyze medication adherence and pharmacotherapy management among older adult patients. We examined how factors such as age, gender, cognitive function, depression and self-efficacy influenced medication adherence. Conducted in routine outpatient practice, not in specialist or institutional settings, the study reflects real-world patient profiles and healthcare access

typical for an ageing population, while simultaneously examines health literacy, depression, self-efficacy, and living situation as potential determinants of adherence.

The main goal of the study was to evaluate adherence to pharmacotherapy among older adults in relation to polypharmacy, cognitive functioning, depressive symptoms, self-sufficiency, and health literacy. Secondary aims included identifying patient strategies for medication management.

2 Methods

This study was reported in accordance with STrengthening the Reporting of OBservational studies in Epidemiology [27] (Supplementary eTable 1). Written informed consent was obtained. This study was conducted in accordance with the Declaration of Helsinki and approved by Medical University of Lodz Ethical Committee (Decision number RNN/84/24/KE on the day of 12.03.2024). Clinical trial number not applicable.

2.1 Study Design and Setting

This cross-sectional study was conducted in three branches of the MEJAMED Family Physician Ambulatory Care in Łódź, Poland, between April of 2024 and June of 2025. The Clinic works under public health care system in Poland and is a standard primary care facility - insured patients may get medical opinion or care upon various health problems free of additional charges. It provides basic laboratory tests, electrocardiogram and physicians evaluation and is followed with medical opinion, drug prescription or specialist care referral.

2.2 Participants

Patients aged ≥60 years at the time of data collection were recruited from previously mentioned three branches of the MEJAMED Family Physician Ambulatory Care in Łódź, Poland. Eligible

participants were primary health care patients, who themselves were responsible for managing their pharmacotherapy. Exclusion criteria included refusal to participate, withdrawal of consent and incomplete data collection – mainly not bringing their medicine to the facility for the review.

2.3 Sample size

A minimum of 208 participants was required to obtain adequate confidence level and margin of error, calculated with an assumed 50% prevalence of non-adherence, 85% confidence level, and 5% margin of error, based on a population of 9.8 million individuals aged ≥60 in Poland necessary to calculate the optimal sample size [Figure 1]. Additional participants were enrolled as needed to compensate for withdrawals and subjects not fulfilling the inclusion criteria and missing data.

2.4 Procedures and Measures

Participants underwent a structured, in-person medication review in primary care clinic, during which all prescribed and non-prescribed drugs brought to the review by patients were documented. Medication management strategies (e.g., pill organizers, alarms, no method) were recorded. Standardized instruments were used for the evaluation of various dimensions: the Mini-Mental State Examination (MMSE) for cognition[28], Geriatric Depression Scale (GDS) for depression[29], General Self-Efficacy Scale (GSES) for self-sufficiency[30], Adherence to Refills and Medications Scale (ARMS) for adherence[31], and HLS-EU-Q16 for health literacy[32]. Further description of these standardized instruments as well as the list of questions used within them are to be found in the Supplement 1.

Variables included sociodemographics, number of medications, education level, living conditions, cognitive level (MMSE), depression severity (GDS), self-sufficiency (GSES), health literacy (HLS-EU-Q16), and adherence (ARMS).

2.5 Statistical analysis

In descriptive statistics, categorical variables were presented with the number of subjects and percentages, whereas numerical variables were displayed with median and inter quartile range. Mann-Whitney U test or Kruskal-Wallis test, and Chi-square test were used for numerical variables and categorical variables, where applicable.

To examine factors associated with adherence to refills and medication, we used binary logistic regression with different adjusted models. Model 1 was age- and gender-adjusted logistic regression. Model 2 was additionally adjusted for education, cohabitation status, number of specialists overlooking the patients, usage of box for drugs and number of daily used medications. Model 3 was fully adjusted logistic regression model. Multicollinearity between independent variables was evaluated with the generalized variance inflation factor. The goodness-of-fit of logistic regression models were assessed with Hosmer-Lemeshow test. Results were presented as odds ratio (OR) and 95% confidence interval (95% CI).

All statistical tests were two tailed with a p-value less than 0.05 considered statistically significant. STATA version 18 MP2 (StataCorp LLC, College Station, Texas, USA) were used to perform the statistical analyses. Missing values were examined, and complete case analysis was applied.

3 Results

3.1 Participant Characteristics

As shown in Table 1, a total of 212 participants were included in the study, stratified by cognitive performance into three groups: normal cognition (MMSE 27-30, n=101), cognitive disorder without dementia (MMSE 24-26, n=57) and mild dementia (MMSE 19-23, n=54). The median age differed significantly across these groups (69.0 [IQR 66-76], 71.0 [IQR 67-77], and 76.0 [IQR 69-83] years,

$p<0.001$). The proportions of women did not differ significantly across the groups, with 76.2%, 66.7%, and 75.9% of women, respectively in these three groups.

Living alone was more frequent among participants with lower MMSE scores (59.3% in MMSE 19-23 vs. 43.6% in MMSE 27-30, $p=0.063$). Education showed a trend toward lower attainment in those with poorer cognitive function: 27.8% in MMSE 19-23 had only basic education compared to 11.9% in MMSE 27-30 ($p=0.053$).

The number of daily medications differed significantly between groups. Participants with MMSE 24-26 used more drugs (median 7 [IQR 5-10]) than those with MMSE 27-30 (median 5 [IQR 3-8], $p=0.028$), whereas the MMSE 19-23 group reported a similar median of 5 (IQR 3-8).

Self-efficacy (GSES) scores were not significantly different across groups). In contrast, health literacy (HLS-EU-Q16) declined significantly with worsening cognitive function: median scores were 13 (10-15), 12 (10-14), and 11 (8-12) for MMSE 27-30, 24-26, and 19-23, respectively ($p=0.001$). Participants with MMSE 19-23 were more likely to fall into the lowest health literacy category (<11 points: 42.6% vs. 25.7% in MMSE 27-30, $p=0.021$).

Depressive symptoms were more frequent in participants with lower MMSE scores: 14.8% in MMSE 19-23 had severe depression ($p=0.046$).

3.2 Adherence to Pharmacotherapy

Adherence, measured by the ARMS, declined with worsening cognition. The proportion of participants adherent to medications was 64.4% in MMSE 27-30, 56.1% in MMSE 24-26, and only 38.9% in MMSE 19-23 ($p=0.010$). Median ARMS scores increased accordingly (15 [IQR 13-16], 15 [IQR 13-18], and 16 [IQR 13-18]; overall $p=0.082$, MMSE 19-23 vs. 27-30, $p=0.028$).

3.3 Regression analysis

Logistic regression models demonstrated a clear association between cognitive impairment and medication adherence (Figure 1). Using the MMSE score of 27-30 as the reference category, participants with moderate cognitive impairment (MMSE 19-23) had substantially reduced odds of adherence (OR = 0.34, 95% CI 0.15-0.78), corresponding to a 66% decrease. Those with mild cognitive impairment (MMSE 24-26) also showed lower adherence, although this association was not statistically significant (OR = 0.79, 95% CI 0.37-1.69).

Several additional variables independently predicted non-adherence. Female participants (OR = 3.32, 95% CI 1.52-7.23) had more than threefold higher odds of adherence than males. Living alone (OR = 0.48, 95% CI 0.23-0.98), taking 5-9 medications daily (OR = 0.34, 95% CI 0.16-0.71), and lower health literacy (HLS-EU-Q16 score 11-13: OR = 0.37, 95% CI 0.17-0.81) were also associated with reduced adherence. In contrast, depression, the number of specialists that participate in care and the use of pill organizers did not show significant associations.

4 Discussion

The primary aim of this study was to evaluate adherence to pharmacotherapy among older adults in relation to cognitive status, polypharmacy, depressive symptoms, self-sufficiency, and health literacy. Our findings clearly demonstrate that cognitive status plays a central role in adherence outcomes. Participants with lower MMSE scores exhibited markedly poorer adherence (38.9% vs. 64.4%), accompanied by reduced health literacy, more severe depressive symptoms, and higher odds of non-adherence (OR 0.34, 95% CI 0.15-0.78). These results underscore that cognitive impairment - together with psychosocial vulnerabilities - substantially disrupts adherence behavior in ageing populations.

Even though there was no exclusion criteria for the severity of dementia, most of the responses came from three groups stratified by MMSE test - normal cognitive functioning, cognitively impaired and mild dementia. It might stem from the fact that people with more severe dementia are unable to visit outpatient care facilities on their own[33]. However, this should not affect the conclusions of the study, as individuals with more severe dementia are unable to care for themselves and require the assistance of others; therefore, in this group, the issue of compliance with recommendations is addressed by the individuals caring for these patients[34].

We found that individuals with cognitive dysfunction but without dementia were prescribed more medications than both cognitively normal participants and those with mild dementia. This pattern likely reflects a combination of higher disease burden and deprescribing tendencies once dementia is recognized - an effect documented in prior research showing medication reduction after dementia diagnosis [35].

The study is the first to assess health literacy in Poland and it shows how literacy and self-sufficiency influence adherence. Declining cognitive function was associated with lower health literacy levels, consistent with evidence that cognitive processes are fundamental to comprehending health information [36]. Because health literacy emerged as a significant correlate of adherence, these findings reinforce the importance of monitoring cognitive decline not only for diagnostic purposes but also for anticipating challenges in managing complex regimens.

Depressive symptoms - another factor central to our primary aim - were more prevalent in participants with cognitive impairment. Depression and cognitive decline share a bidirectional relationship, which may complicate motivation, concentration, and planning needed for consistent medication use [37]. Although depressive symptoms were not a direct predictor of adherence in our

model, their co-occurrence with cognitive decline suggests that emotional health remains an important contextual factor.

Taken together, our findings support the hypothesis that medication adherence worsens with declining cognitive ability, even after accounting for polypharmacy, depressive symptoms, functional status, and health literacy. People with mild dementia had significantly poorer adherence than cognitively healthy individuals, and a similar - though not statistically significant - trend was observed in those with cognitive impairment. This aligns with previous research linking cognitive deficits to difficulties in medication management [38-40].

The secondary aim of the study was to identify patient strategies used to manage medications. Our findings provide indirect insights into this area: while polypharmacy (5-9 drugs) was associated with the highest non-adherence, hyperpolypharmacy (≥10 drugs) demonstrated better adherence. This is consistent with evidence that pillboxes, electronic reminders, and caregiver involvement enhance adherence in complex regimens [41-43]. These observations highlight that strategy use, rather than medication count alone, may be critical to sustaining adherence in high-burden regimens.

Within evaluating how polypharmacy relates to adherence, our results show that intermediate medication burden posed the greatest adherence challenge, which aligns with literature consistently demonstrating that polypharmacy increases treatment complexity and risk of non-adherence [44]. Additionally, deprescribing observed among individuals with dementia - a process confirmed in prior studies [45] - likely influences both medication count and adherence patterns.

Our aim also included evaluating self-sufficiency and psychosocial determinants. Consistent with previous research, living alone and low health literacy were associated with poorer adherence, emphasizing the role of social support and informational capacity in successful medication

management [46-48]. These factors interacted with cognitive status, suggesting that adherence is shaped by a combination of cognitive, functional, and social vulnerabilities.

Although lifestyle and psychosocial interventions can improve cognitive function and mood - which indirectly support medication self-management - they cannot replace essential pharmacotherapy for chronic diseases [49-50]. Nevertheless, they may complement adherence strategies by enhancing cognitive reserve and emotional wellbeing.

Overall, by directly addressing the study's aims, our results indicate that improving adherence among older adults requires prioritizing cognitive assessment, simplifying polypharmacy where possible, and strengthening patients' health literacy and social support structures. Interventions should be tailored to cognitive and functional needs and integrated into daily routines, as suggested by broader evidence on cognitive support strategies [51]. The identification of strategy use - particularly organizational tools and caregiver involvement - further emphasizes the importance of structured support in medication self-management. Together, these insights highlight the necessity of multifaceted approaches to ensure safe and effective pharmacotherapy in cognitively declining populations.

One of the study's limitations was the selectivity of the respondents' geographical origins. The research was conducted in the large city of Łódź (approximately 740,000 inhabitants), as the clinics where the surveys were administered were located in the city center. This setting limited participation from individuals living in suburban and rural areas. Similar limitation came with convenience sample used for the study. Finally, it is important to acknowledge the fact that the data gathered from the patient was subjective and even though the survey was gathered in an anonymous manner, some patients would still be prone to lie about their adherence and other results.

5 Conclusions

1. Cognitive decline is strongly linked to worse medication adherence.
2. Adherence decreases progressively with worsening cognition.
3. Lower health literacy significantly increased the risk of non-adherence.
4. Living situation and medication burden matter.
5. Women had significantly higher odds of adherence than men.
6. Some expected factors were not significant.

6 Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

7 Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by Medical University of Lodz Ethical Committee (Decision number RNN/84/24/KE on the day of 12.03.2024).

8 Consent for publication

Not applicable.

9 Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

10 Competing interest

The authors declare that they have no competing interests.

11 Funding

There has been no funding acquired for this study.

12 Authors contributions

WT – Data Curation, Investigation, Project Administration, Writin-Original draft, Writing-review and editing; MTH – Data Curation, Formal Analysis, Software, Visualisation, Writing-review and editing; JKT – Investigation, Writing-original draft; DR – Conceptualisation, Methodology, Project Administration, Supervision, Writing-review and editing; PK – Conceptualisation, Methodology, Project Administration, Supervision, Writing-review and editing. All authors read and approved the final manuscript.

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15 Figures, tables and additional files

Finite population: $n' = \frac{n}{1 + \frac{z^2 \times \hat{p}(1-\hat{p})}{\varepsilon^2 N}}$

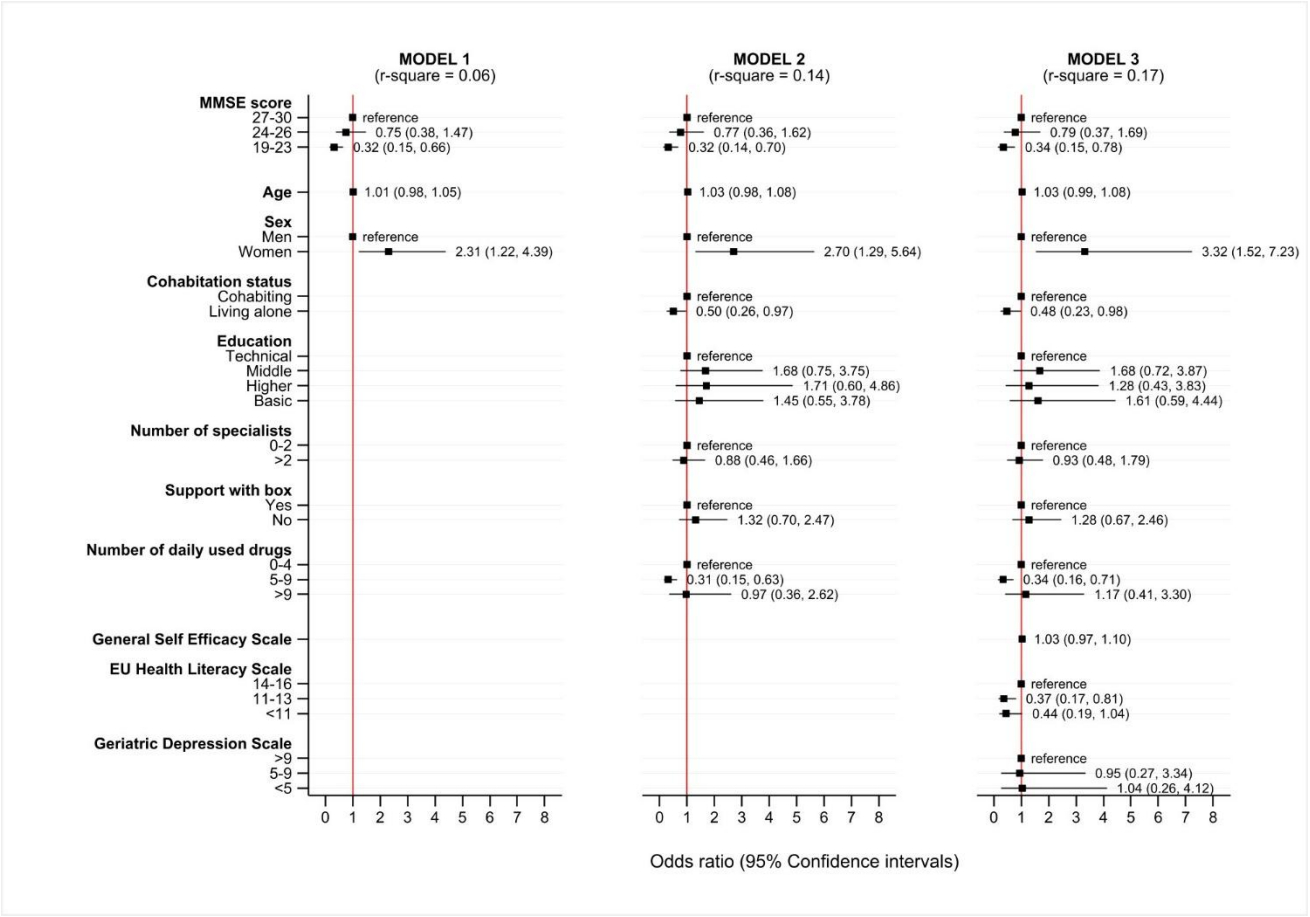
where
z is the z score
ε is the margin of error
N is the population size
p̂ is the population proportion



490

491 **Figure 1.** Mathematical formula for sample size calculation, https://www.calculator.net/sample-size-

492 calculator.html



493

494 **Figure 2.** Factors associated with adherence to pharmacotherapy among older adults. Logistic

495 regression models were used to estimate odds ratios (ORs) with 95% confidence intervals. Model 1

was adjusted for age and gender; Model 2 was additionally adjusted for education, cohabitation status, number of specialists, support with pill boxes, and number of daily medications; Model 3 was fully adjusted, including self-efficacy, health literacy, and depression.

Table 1. Baseline characteristics of participants (n = 212) according to cognitive performance (MMSE categories 27–30, 24–26, 19–23). Data are presented as median (interquartile range) or number (percentage).

Table 2. Association between cognitive performance and adherence to pharmacotherapy. Results are presented as odds ratios (ORs) with 95% confidence intervals derived from logistic regression models.

Supplementary Files

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- 1795758SupMaterial.zip